

BIRD ET AL. - U.S. Patent Appl. No. 10/019,236

II. REMARKSPreliminary Remarks

Reconsideration and allowance of the present application based upon the foregoing amendment and following remarks are respectfully requested. Claims 1, 4-12, 15, 16, 23-26, 28-30, 32-36, 39-49, and 51-78 are currently pending and at issue in the application.

Amended claim 52 is directed to the method of claim 42 wherein the resistant starch is a resistant starch. Claim 52 was amended to correct a typographical error regarding the dependency of the claim and not for any reasons of patentability.

In paragraph 2 of the official action, the examiner requested an abstract of the disclosure be submitted as required under 37 C.F.R. §1.72(b). The applicants submit herewith an abstract (on a separate page).

This response is timely filed as it is accompanied by a petition for an extension of time to file in the first month and the requisite fee.

The applicants do not intend by these or any amendments to abandon subject matter of the claims as originally filed or later presented, and reserve the right to pursue such subject matter in continuing applications.

Patentability RemarksRejection Under 35 U.S.C. §112, Second Paragraph

In paragraphs 5 and 6 of the official action, the examiner rejected claims 7-10, 12, and 70-72 under 35 U.S.C. §112, second paragraph, for allegedly being indefinite. Specifically, the examiner alleged that "acetate, propionate, butyrate, etc" are not single chain fatty acids but are esters. The examiner further asserted that claim 12 fails to contain sufficient antecedent basis for the term "omega 3 fatty acid."

In order to expedite prosecution and without prejudice to the applicants' right to seek broader claims in a continuing application, claims 9 and 10 have been canceled without prejudice thereby obviating the rejection of these claims. Amended claim 7 is directed to an enteral formulation for nasogastric delivery as in claim 6 wherein the SCFA comprises a carbon chain length between 1 and 10. Amended claim 8 is directed to an enteral formulation for nasogastric delivery as in claim 6 wherein the SCFA comprises a chain length between 2 and 4. Amended claim 70 has been amended to be directed to the method of claim 39.

BIRD ET AL. - U.S. Patent Appl. No. 10/019,236

wherein the fatty acid is a short chain fatty acid (SCFA). Amended claim 71 has been amended to be directed to the method of claim 39, wherein the SCFA comprises a carbon chain length between 1 and 10. Amended claim 72 is directed to the method of claim 39, wherein the SCFA comprises a carbon length between 2 and 4. Support for amended claims 7, 8, and 70-72 can be found throughout the specification, for example, on page 4, line 31 to page 5, line 4.

The applicants submit that claims 7, 8, and 70-72 no longer refer to esters and are now directed to various short chain fatty acids used in the enteral formulations and methods thereof for nasogastric delivery. Claim 12 now draws its dependency from claim 11 and thus the term "omega 3 fatty acid" has proper antecedent basis. In view of the foregoing amendment and remarks, the applicants respectfully submit that the rejection of claims 7-10, 12, and 70-72 under 35 U.S.C. §112, second paragraph, has been overcome and should be withdrawn.

Judicially Created Doctrine of Obviousness-Type Double Patenting

In paragraphs 3 and 4 of the official action, the examiner rejected claims 1, 4-12, 15, 16, 23-26, 28-30, 32-36, 39-49, and 51-78 under the judicially created doctrine of obviousness-type double patenting over claims 1-118 of U.S. Patent No. 5,840,860 (hereafter Annison *et al.*) in view of U.S. Patent No. 5,723,446 (hereafter Gray *et al.*). Specifically, the examiner asserted that the '860 patent claims a method for delivering fatty acid to the colon via a carbohydrate carrier. The examiner further alleged that although the '860 patent does not claim a formulation (fatty acid + carbohydrate etc.) comprising a protein source, carbohydrate source, and lipid source, the '446 patent discloses such formulations, which meet the requirements of intensive care patients who may have compromised absorption capacity, it would have been obvious to provide (and be motivated with a reasonable expectation of success) a method to deliver fatty acids to the colon by administering a formulation comprising fatty acids covalently bonded to carbohydrates and nutrient formulations in view of the Gray *et al.* and Annison *et al.*

With regard to the remaining pending claims, the applicants submit that Gray *et al.* neither teach nor suggest the applicants' claimed invention, *i.e.*, an enteral formulation for nasogastric delivery comprising (a) an amino acid source, (b) a carbohydrate source, (c) a lipid source, and (d) a fatty acid delivery agent, being a fatty acid covalently bonded to a carrier molecule by a bond hydrolysable in the colon to thereby release the fatty acid, the

BIRD ET AL. - U.S. Patent Appl. No. 10/019,236

covalent bonding providing a protective effect to both the carrier and fatty acid from covalent bonding providing a protective effect to both the carrier and fatty acid from degradation in the stomach or small intestine, said carrier being any one of a starch, a non-starch polysaccharide, or oligosaccharide the fatty acid delivery agent being present in the formulation range of 0.25% w/v through to 5% w/v, and wherein the formulation can be delivered through an enteral feeding tube.

More particularly, the applicants submit that Gray *et al.* does not teach or suggest that a carrier molecule (*i.e.*, a non-starch polysaccharide) is complexed with a fatty acid molecule such as short chain fatty acids. Gray *et al.*'s reference to "soluble or insoluble fiber to provide anti-diarrhoeal characteristics" at column 4, lines 29-33 fails to quantify the amount of fiber or teach what form the fiber should be processed in order to reach the colon and be effective. If one of skill in the art were to interpret this passage in Gray *et al.*, the standard fiber preparations would be introduced in the digestive tract in limited quantities through an enteral (nasogastric) tube in comparison to the applicants' teachings. Further, Gray *et al.* fails to address the viscosity problems associated with fiber carriers of fatty acids in enteric tubes. In contrast, the applicants teach that a fatty acid delivery agent, instead of a fiber component, is superior because delivery of an adequate quantity of usual fiber components gives rise to viscosity problems via an enteral tube. In order to avoid clogging or viscosity problems, an enteral tube with the fiber/fatty acid preparations as taught in Grey *et al.* would require large volumes of diluent, which would have adverse physiological effects on the patient. Accordingly, given the viscosity constraints inherent in providing higher levels of fiber in formulations derived via enteral tubes, the applicants submit it would not have been obvious to one of skill to use the claimed fatty acid delivery agents in place of the soluble/insoluble fiber and/or carob pod powder or tannin extract taught in Grey *et al.*

Furthermore, there is no teaching or suggestion in Grey *et al.* that delivery of fatty acids through a enteral (nasogastric) tube could be achieved by reducing the concentration of the fatty acid delivery agent to a level of 5% w/v, and yet provide beneficial effects as presented in Examples 4 and 5 and page 16, lines 11-29. The applicants' examples disclose the unexpected results that the claimed carriers linked covalently to complex fatty acids can replace normal fiber supplements in order to provide a colonic benefit of SCFA or other fatty acids (and thus alleviating nutritional deficiencies of the large bowel) via an enteral tube.

The applicants believe that the examiner further cited Annison *et al.* for the alleged teaching that this reference discloses a fatty acid delivery system comprised of a fatty acid source wherein the carbohydrate serves as the carrier wherein one of the preferred carriers is

BIRD ET AL. - U.S. Patent Appl. No. 10/019,236

starch. The applicants submit that this secondary reference does little to overcome the failings of the primary document, Gray *et al.*

The applicants' claimed enteral formulation, in contrast, has a maximum fatty acid delivery agent percentage of only 5%. One of skill in the art would not expect a 5% complex fatty acid delivery agent concentration to be an adequate amount to provide the colonic benefits of the SCFA or other fatty acids as a replacement of normal fiber supplements. Yet, in fact, the applicants submit that for the first time their teachings give the unexpected result of a quantum increase in the capacity to alleviate nutritional deficiencies in the large bowel via the enteral tube by using the recited fatty acid delivery agents at a 0.25% to 5% weight ratio to the overall formulation.

In contrast, Annison *et al.* did not teach that the fatty acid delivery agent could be administered as a nasogastric formulation. Also, Annison *et al.* fail to indicate that delivery through a nasogastric tube can be achieved by decreasing the concentration of the fatty acid delivery agent (starch) (*i.e.* to levels of 0.25 to 5.0%) relative to the levels shown in the examples of Annison *et al.*, and yet still provide a beneficial effect as assessed by the indicators shown in the data of the present invention. In fact, the levels of the fatty acid delivery agent starch disclosed in Annison *et al.*'s *in vivo* experiments (Tables 3 and 11) were calculated to be 15%, which would clog the enteral tube. Specifically, the enteral formulation of Annison *et al.* would be undeliverable using a enteral tube for delivery via the nasogastric route with the 15% percent of starch in the fatty acid deliver agents due the viscosity constraints inherent in a 15% fatty acid delivery agent level. Thus Annison *et al.* teaches a percent weight/ratio of starch (as the fatty acid delivery agent) that actually teaches away from enteral formulation (0.25 to 5.0% weight ration of fatty acid delivery agent) disclosed by the applicants.

In furtherance that there is no disclosure of the low concentrations of the fatty acid delivery agent in formulations for ingestion or that such low concentrations can give rise to a benefit, the applicants further submit that there is no motivation to combine the Gray *et al.* or Annison *et al.* in the alleged double patenting obviousness-type double patenting. The applicants submit that Gray *et al.* teach nasogastric formulations for application to burn or trauma patients. In contrast, Annison *et al.* teach preparations containing fatty acids (with a 15% fatty acid delivery agent levels vs. applicants 0.25% to 5.0% weight ration of fatty acid delivery agent) resistant to degradation that are formulated for foods, pellets, and powders. Annison *et al.* fail to teach or suggest that their 15% fatty acid delivery agent for foods would

BIRD ET AL. - U.S. Patent Appl. No. 10/019,236

be useful or even possible for formulations via nasogastric delivery. Similarly, there is no teaching or suggestion in Gray *et al.* that fiber delivery to the colon was deficient when using enteral formulations for nasogastric delivery prior to the applicants' invention. Gray *et al.* only addresses the delivery of high levels of fatty acids for a high caloric density intake, but does not address fiber deficiencies to the colon.

The applicants further submit that neither Gray *et al.* nor Annison *et al.*, either alone or in combination, teach the specific formulations of 0.25% to 5% of short chain fatty acids for effective delivery of fiber to the colon. The use of applicants' enteral formulations provide a boost to colonic health by inducing colonocyte production. Colonocyte production is neither taught nor suggested by Gray *et al.* or Annison *et al.*. In contrast, Gray *et al.* and Annison *et al.* together only teach delivery formulations using resistant starch or other resistant fiber which cannot be effectively fermented in the colon. One of skill in the art would have been unable to appreciate in view of these teachings that the use of lesser concentrations of short chain fatty acids, as set forth in the claimed invention, would still deliver an effective amount of fiber to the bowel resulting in butyrate (for example) production via fermentation. The applicants invention (formulations using a low concentration of short length fatty acids) is novel and unobvious because the density of butyrate created by the fermentation of applicants formulation effectively delivers an unexpected higher level of butyrate than the level of butyrate delivered by Gray *et al.* and Annison *et al.* disclosed formulations (*i.e.*, resistant starch).

Accordingly, the applicants respectfully submit that one of skill in the art would not be directed to an enteral formulation for nasogastric delivery comprising (a) an amino acid source, (b) a carbohydrate source, (c) a lipid source, (d) a fatty acid delivery agent, being a fatty acid covalently bonded to a carrier molecule by a bond hydrolysable in the colon to thereby release the fatty acid, the covalent bonding providing a protective effect to both the carrier and fatty acid from degradation in the stomach or small intestine, said carrier being any one of a start, a non-starch polysaccharide, or oligosaccharide, wherein the fatty acid delivery agent being present in the formulation range of 0.25% w/v through to 5% w/v, and wherein the formulation can be delivered through an enteral feeding tube in view of Annison *et al.*

In summary, the applicants submit the primary reference, Gray *et al.*, either alone or in combination with Annison *et al.*, neither teach nor suggest the applicants' claimed invention. Accordingly, without such teaching or suggestion, the examiner has not

BIRD ET AL. - U.S. Patent Appl. No. 10/019,236

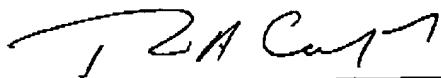
established a *prima facie* case of obviousness. In view of the foregoing remarks, the applicants respectfully submit that the rejection of claims 1, 4-12, 15, 16, 23-26, 28-30, 32-36, 39-49, and 51-78 under the judicially created doctrine of obviousness-type double patenting should be withdrawn.

BIRD ET AL. - U.S. Patent Appl. No. 10/019,236

III. CONCLUSION

In view of the foregoing, the claims are now believed to be in form of allowance, and such action is hereby solicited. If any point remains at issue which the examiner feels may be best resolved through a personal or telephone interview, please contact the undersigned at the telephone number below.

Respectfully submitted,
PILLSBURY WINTHROP LLP



Thomas A. Cawley, Jr., Ph.D.
Reg. No. 40,944
Tel. No. (703) 905-2144

TAC/PAJ
P.O. Box 10500
McLean, VA 22102
(703) 905-2000